ATTACHMENT E

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Chemistry of Fatty Acids

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1. INTRODUCTION

Fatty acids, esterified to glycerol, are the main constituents of oils and fats. The industrial exploitation of oils and fats, both for food and oleochemical products, is based on chemical modification of both the carboxyl and unsaturated groups present in fatty acids. Although the most reactive sites in fatty acids are the carboxyl group and double bonds, methylenes adjacent to them are activated, increasing their reactivity. Only rarely do saturated chains show reactivity. Carboxyl groups and unsaturated centers usually react independently, but when in close proximity, both may react through neighboring group participation. In enzymatic reactions, the reactivity of the carboxyl group can be influenced by the presence of a nearby double bond.

The industrial chemistry of oils and fats is a mature technology, with decades of experience and refinement behind current practices. It is not, however, static. Environmental pressures demand cleaner processes, and there is a market for new products. Current developments are in three areas: "green" chemistry, using cleaner processes, less energy, and renewable resources; enzyme catalyzed reactions, used both as environmentally friendly processes and to produce tailor-made products; and novel chemistry to functionalize the carbon chain, leading to new

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compounds. Changing perceptions of what is nutritionally desirable in fat-based products also drives changing technology; interesterification is more widely used and may replace partial hydrogenation in the formulation of some modified fats.

The coverage in this chapter is necessarily selective, focusing on aspects of fatty acid and lipid chemistry relevant to the analysis and industrial exploitation of oils and fats. The emphasis is on fatty acids and acylglycerols found in commodity oils and the reactions used in the food and oleochemical industries. The practical application of this chemistry is dealt with in detail in other chapters. Current areas of research, either to improve existing processes or to develop new ones, are also covered, a common theme being the use of chemical and enzyme catalysts. Compounds of second-row transition metals rhodium and ruthenium and the oxides of rhenium and tungsten have attracted particular interest as catalysts for diverse reactions at double bonds. Recent interest in developing novel compounds by functionalizing the fatty acid chain is also mentioned. To date, few of these developments have found industrial use, but they suggest where future developments are likely. A number of recent reviews and books cover and expand on topics discussed here (1–10).

2. COMPOSITION AND STRUCTURE

2.1. Fatty Acids

Fatty acids are almost entirely straight chain aliphatic carboxylic acids. The broadest definition includes all chain lengths, but most natural fatty acids are C_4 to C_{22}, with C_{18} most common. Naturally occurring fatty acids share a common biosynthesis. The chain is built from two carbon units, and *cis* double bonds are inserted by desaturase enzymes at specific positions relative to the carboxyl group. This results in even-chain-length fatty acids with a characteristic pattern of methylene interrupted *cis* double bonds. A large number of fatty acids varying in chain length and unsaturation result from this pathway.

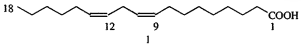
Systematic names for fatty acids are too cumbersome for general use, and shorter alternatives are widely used. Two numbers separated by a colon give, respectively, the chain length and number of double bonds: octadecenoic acid with 18 carbons and 1 double bond is therefore 18:1. The position of double bonds is indicated in a number of ways: explicitly, defining the position and configuration; or locating double bonds relative to the methyl or carboxyl ends of the chain. Double-bond position relative to the methyl end is shown as n-x or ωx, where x is the number of carbons from the methyl end. The n-system is now preferred, but both are widely used. The position of the first double bond from the carboxyl end is designated Δx. Common names (Table 1) may be historical, often conveying no structural information, or abbreviations of systematic names. Alternative repre-

TABLE 1. Fatty Acids in Commodity Oils and Fats. (a) Nomenclature and Structure.

Fatty acid	Common name	Formula	Chain length
4:0	butyric	$CH_3(CH_2)_2CO_2H$	short
6:0	caproic	$CH_3(CH_2)_4CO_2H$	short
8:0	caprylic	$CH_3(CH_2)_6CO_2H$	short/medium
10:0	capric	$CH_3(CH_2)_8CO_2H$	medium
12:0	lauric	$CH_3(CH_2)_{10}CO_2H$	medium
14:0	myristic	$CH_3(CH_2)_{12}CO_2H$	medium
16:0	palmitic	$CH_3(CH_2)_{14}CO_2H$	
18:0	stearic	$CH_3(CH_2)_{16}CO_2H$	
18:1 9c	oleic	$CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2H$	
18:2 9c12c	linoleic	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6CO_2H$	
18:3 9c12c15c	α-linolenic	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6CO_2H$	
22:1 13c	erucic	$CH_3(CH_2)_7CH{=}CH(CH_2)_{11}CO_2H$	long
20:5 5c 8c11c14c17c	EPA*	$CH_3CH_2(CH{=}CHCH_2)_5(CH_2)_2CO_2H$	long
22:6 4c7c10c13c16c19c	DHA*	$CH_3CH_2(CH{=}CHCH_2)_6CH_2CO_2H$	long

*Abbreviations of the systematic names eicosapentaenoic acid and docosahexaenoic acid.

sentations of linoleic acid (**1**) are 9*Z*,12*Z*-octadecadienoic acid; 18:2 9c12c; 18:2 n-6; 18:2 ω6; 18:2 Δ9,12; or $CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$.



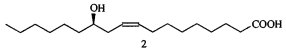
The terms *cis* and *trans*, abbreviated *c* and *t*, are used widely for double-bond geometry; as with only two substituents, there is no ambiguity that requires the systematic *Z*/*E* convention. An expansive discussion of fatty acid and lipid nomenclature and structure appears in Akoh and Min (1).

TABLE 1. (b) Occurrence.

Fatty Acid	Significant Sources
4:0	butter, dairy fats
6:0	(coconut, palm kernel)
8:0	(coconut, palm kernel)
10:0	(coconut, palm kernel)
12:0	coconut, palm kernel
14:0	coconut, palm kernel
16:0	cottonseed, palm
18:0	cocoa butter, tallow
18:1 9c	cottonseed, olive, palm, rape
18:2 9c12c	corn, sesame, soybean, sunflower
18:3 9c12c15c	linseed
20:1 13c	high erucic rape
20:5 5c8c11c14c17c	fish and animal fats
22:6 4c7c10c13c16c19c	fish and animal fats

Over 1000 fatty acids are known, but 20 or less are encountered in significant amounts in the oils and fats of commercial importance (Table 1). The most common acids are C_{16} and C_{18}. Below this range, they are characterized as short or medium chain and above it as long-chain acids.

Fatty acids with *trans* or non-methylene-interrupted unsaturation occur naturally or are formed during processing; for example, vaccenic acid (18:1 11*t*) and the conjugated linoleic acid (CLA) rumenic acid (18:2 9*t*11*c*) are found in dairy fats. Hydroxy, epoxy, cyclopropane, cyclopropene acetylenic, and methyl branched fatty acids are known, but only ricinoleic acid (12(*R*)-hydroxy-9Z-octadecenoic acid) (2) from castor oil is used for oleochemical production. Oils containing vernolic acid (12(*S*),13(*R*)-epoxy-9Z-octadecenoic acid) (3) have potential for industrial use.



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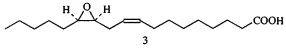

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Typical fatty acid composition of the most widely traded commodity oils is shown in Table 2.

TABLE 2. Fatty Acid Content of the Major Commodity Oils (wt%).

	16:0 (wt%)	18:1 (wt%)	18:2 (wt%)	18:3 (wt%)	Other [Fatty Acid (wt%)]
butter	28	14	1	1	4:0 (9); 6:0–12:0 (18); 14:0 (14) + odd chain and *trans*
castor	1	3	4		18:1(OH) (90)
coconut	9	6	2		8:0 (8); 10:0 (7); 12:0 (48); 14:0 (18)
corn	13	31	52	1	
cottonseed	24	19	53		
fish*	14	22	1		16:1 n-7 (12); 20:1 n-9 (12); 22:1 n-11 (11); 20:5 n-3 (7); 22:6 n-3 (7)
groundnut (peanut)	13	37	41		C_{20}–C_{24} (7)
lard	27	44	11	1	14:0 (2) 18:0 (11) + long and odd chain
linseed	6	17	14	60	
olive	10	78	7		
palm	44	40	10		
palm kernel	9	15	2		8:0 (3); 10:0 (4); 12:0 (49); 14:0 (16)
rape**	4	56	26	10	
sesame	9	38	45		18:0 (6)
soybean	11	22	53	8	
sunflower	6	18	69		18:0 (6)
tallow	26	31	2		14:0 (6) 18:0 (31) + long and odd chain

Typical midrange values shown; the balance are minor components. Data from (9).
*Cod liver oil.
**Low-erucic-acid rape, e.g., Canola.

Most commodity oils contain fatty acids with chain lengths between C_{16} and C_{22}, with C_{18} fatty acids dominating in most plant oils. Palm kernel and coconut, sources of medium-chain fatty acids, are referred to as lauric oils. Animal fats have a wider range of chain length, and high erucic varieties of rape are rich in this C_{22} monoene acid. Potential new oil crops with unusual unsaturation or additional functionality are under development. Compilations of the fatty acid composition of oils and fats (6, 9, 11, 12) and less-common fatty acids (13) are available.

The basic structure, a hydrophobic hydrocarbon chain with a hydrophilic polar group at one end, endows fatty acids and their derivatives with distinctive properties, reflected in both their food and industrial use. Saturated fatty acids have a straight hydrocarbon chain. A *trans*-double bond is accommodated with little change in shape, but a *cis* bond introduces a pronounced bend in the chain (Fig. 1).

In the solid phase, fatty acids and related compounds pack with the hydrocarbon chains aligned and, usually, the polar groups together. The details of the packing, such as the unit cell angles and head-to-tail or head-to-head arrangement depend on the fatty acid structure (Fig. 2).

The melting point increases with chain length and decreases with increased unsaturation (Table 3). Among saturated acids, odd chain acids are lower melting than adjacent even chain acids. The presence of *cis*-double bonds markedly lowers the melting point, the bent chains packing less well. *Trans*-acids have melting points much closer to those of the corresponding saturates. Polymorphism results in two or more solid phases with different melting points. Methyl esters are lower melting than fatty acids but follow similar trends.

Fatty acid salts and many polar derivatives of fatty acids are amphiphilic, possessing both hydrophobic and hydrophilic areas within the one molecule. These are surface-active compounds that form monolayers at water/air and water/surface interfaces and micelles in solution. Their surface-active properties are highly dependent on the nature of the polar head group and, to a lesser extent, on the length of the alkyl chain. Most oleochemical processes are modifications of the carboxyl group to produce specific surfactants.

TABLE 3. Melting Points of Some Fatty Acids and Methyl Esters Illustrating the Effect of Chain Length and Unsaturation.

Fatty acid	Melting Point (°C)	Fatty Acid	Melting Point (°C)
16:0	62.9 (30.7)		
17:0	61.3 (29.7)		
18:0	70.1 (37.8)		
18:1 9*c*	16.3, 13.4	18:1 9*t*	45
18:2 9*c*12*c*	−5	18:2 9*t*12*t*	29
19:0	69.4 (38.5)		
20:0	76.1 (46.4)		

Values for methyl esters in parenthesis.
Data from (8) and (9).

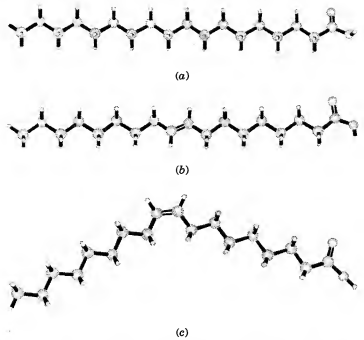


Figure 1. "Ball and stick" models of (a) stearic acid, 18:0; (b) elaidic acid, 18:1 9t; and (c) oleic acid 18:1 9c. All three lie flat in the plane of the paper. The cis double bond causes a distinct kink in the alkyl chain of oleic acid.

2.2. Acylglycerols

Fatty acids in oils and fats are found esterified to glycerol. Glycerol (1,2,3-trihydroxypropane) is a prochiral molecule. It has a plane of symmetry, but if the primary hydroxyls are esterified to different groups, the resulting molecule is chiral and exists as two enantiomers. The stereospecific numbering system is used to

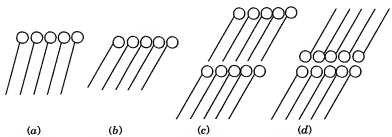


Figure 2. Simplified diagram shows packing patterns of fatty acids in the solid phase. (a) and (b): Hydrocarbon tails (straight lines) aligned at different angles to the line of the polar head groups (circles). (c): Head to tail packing. (d): Head to head packing.

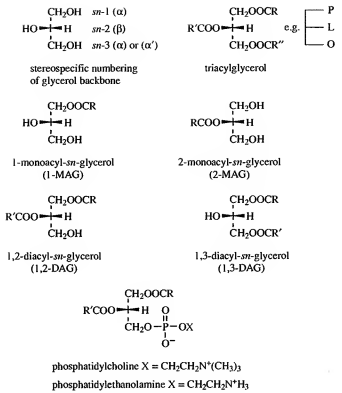


Figure 3. Structure and stereospecific numbering of acylglycerols.

distinguish between enantiomers. The Fischer projection of glycerol is drawn with the backbone bonds going into the paper and the hydroxyl on the middle carbon to the left. The carbons are then numbered 1 to 3 from the top (Figure 3). The prefix *sn-* (for stereospecific numbering) denotes a particular enantiomer, *rac-* an equal mixture of enantiomers, and *x-* an unknown stereochemistry. In an asymmetric environment such as an enzyme binding site, the *sn*-1 and *sn*-3 groups are not interchangeable and reaction will only occur at one position. Simplified structures are often used; e.g., 1-palmitoyl-2-linoleoyl-3-oleoyl-*sn*-glycerol is abbreviated to PLO or drawn as shown in Figure 3.

Storage fats (seed oils and animal adipose tissue) consist chiefly (~98%) of triacylglycerols, with the fatty acids distributed among different molecular species. With only two fatty acids, a total of eight triacylglycerol isomers are possible, including enantiomers (Table 4). A full analysis of triacylglycerol molecular species is a major undertaking, and for some oils, there are still technical difficulties to be resolved. More commonly, triacylglycerols are distinguished by carbon number (the sum of the fatty acid chain lengths) or unsaturation, using GC or HPLC for analysis. The number of isomers increases as the cube of the number of fatty acids;

TABLE 4. Molecular Species of Triacylglycerols Containing only Palmitic and Oleic Acid.

	PPP	POP	PPO	OPP	POO	OOP	OPO	OOO
enantiomers			*	*	**	**		
carbon number	48	50	50	50	52	52	52	54
double bonds	0	1	1	1	2	2	2	3

Different methods of analysis will give different and often incomplete information about such a mixture. GC analysis will separate molecular species by carbon number (sum of fatty acid chain lengths). Silver-ion HPLC will separate by number of double bonds. Stereospecific analysis measures the proportions of fatty acids at the *sn*-1, *sn*-2, and *sn*-3 positions, but it does not detect individual molecular species.

hence, even in oils with a simple fatty acid composition, many molecular species of triacylglycerol may be present.

Most natural triacylglycerols do not have a random distribution of fatty acids on the glycerol backbone. In plant oils, unsaturated acids predominate at the *sn*-2 position, with more saturated acids at *sn*-1 and *sn*-3. The distribution of fatty acids at the *sn*-1 and *sn*-3 positions is often similar, although not identical. However, a random distribution between these two positions is often assumed as full stereospecific analysis is a time-consuming specialist procedure. In animal fats, the type of fatty acid predominating at the *sn*-2 position is more variable; for example, palmitate may be selectively incorporated as well as unsaturated acids (Table 5).

Only oils that are rich in one fatty acid contain much monoacid triacylglycerol, for example, olive (Table 5), sunflower, and linseed oils containing OOO, LLL, and LnLnLn, respectively. Compilations of the triacylglycerol composition of commodity and other oils are available (8, 9).

The melting behavior of triacylglycerols generally reflects that expected from the fatty acid composition; triacylglycerols rich in long-chain and saturated acids

TABLE 5. Contrasting Triacylglycerol Composition of Some Commodity Oils [Molecular Species (wt%)].

Cocoa butter	Coconut	Lard	Olive	Soybean
POP (18-23)	12,12,8 (12)	PPSt (2)	OOL (11)	LnLL (7)
POSt (36-41)	12,12,10 (6)	StPSt (2)	OOO (43)	LnLO (5)
StOSt (23-31)	12,12,12 (11)	PPO (8)	POP (3)	LLL (15)
	12,12,14 (11)	StOP (13)	POL (4)	LLO (16)
unsymmetrical	14,12,8 (9)	POO (5)	POO (22)	LLS (13)
e.g., SSO <1%		StOO (6)	StOO (5)	LOO (8)
		OPO (18)		LOS (12)
		StPL (2)		OOS (5)
		OOO (12)		
		OPL (7)		

L—linoleic; Ln—linolenic; O—oleic; P—palmitic; S—saturate; St—stearic; 8—8:0; 10—10:0; 12—12:0 (lauric); 14—14:0.
Analysis by methods that do not distinguish all isomers; only major components are listed.
Data from (6).

are high melting, and those rich in polyunsaturated acids are lower melting. However, the situation is complicated by the possibility that the fatty acids can be distributed in different molecular species with different melting points. Oils with similar fatty acid composition may have different solid fat content, polymorphic forms, and melting behavior as a result of a different triacylglycerol composition.

Mono- and diacylglycerols (Figure 3) are not significant components of good quality oils, but elevated levels may be found in badly stored seeds, resulting from the activity of lipolytic enzymes. These compounds are produced industrially by partial hydrolysis or glycerolysis of triacylglycerols for use as food grade emulsifiers. Mono- and diacylglycerols readily isomerize under acid or base catalysis and are normally produced as an equilibrium mixture in which 1(3)-monoacylglycerols or 1,3-diacylglycerols predominate.

Phospholipids (Figure 3) are constituents of membranes and are only minor components of oils and fats, sometimes responsible for cloudiness. They are usually removed during degumming, the residue from soybean oil processing being a source of phospholipids used as food emulsifiers. The term "lecithin" is used very loosely for such material, and it may variously mean phosphatidylcholine, mixed glycerophospholipids, or crude phospholipid extracts from various sources. Where possible, more specific nomenclature or the source and purity should be used (14).

2.3. Bulk Properties

Saponification value and iodine value. Oils and fats are now characterized mainly by their fatty acid composition determined by gas chromatography, replacing the titrimetric and gravimetric assays used previously. However, the saponification value (SV) or equivalent (SE) and iodine value (IV) are still used in specifications and to monitor processes. SE, expressed as grams of fat saponified by one mole of potassium hydroxide, is an indication of the average molecular weight and hence chain length, whereas the IV, expressed as the weight percent of iodine consumed by the fat in a reaction with iodine monochloride, is an index of unsaturation (Table 6). Standard analytical methods are available (15), but these parameters are now often calculated from the fatty acid composition, assuming that the sample is all triacylglycerol (15). Indirect measurement of IV (16, 17) and SV (17) (as well as peroxide and *trans*-content) using FT-NIR spectroscopy have been developed for real-time process monitoring.

Unsaponifiable matter. Oils and fats contain variable amounts of sterols, hydrocarbons, tocopherols, carotenoids, and other compounds, collectively referred to as unsaponifiable matter because they do not produce soaps upon hydrolysis (Table 6). The sterol and tocopherol composition of commodity oils is discussed in another chapter. Some of these minor components are removed during refining, and the resulting concentrates may be useful byproducts, for example, tocopherol antioxidants. Characteristic fingerprints of minor components, particularly phytosterols and tocopherols, are also used to authenticate oils and detect adulteration (18).

TABLE 6. Saponification Equivalent (SE), Saponification Value (SV), Iodine Value (IV), and Unsaponifiable Matter of Some Commodity Oils.

	SE* (g oil/mol KOH)	SV (mg KOH/g oil)	IV (100 × g iodine/g oil)	Unsaponifiable matter (wt%)
butter	242–267	210–232	26–40	<0.5
castor	300–319	176–187	81–91	
coconut	212–226	248–265	6–11	<1.5
corn	288–300	187–195	107–128	1–3
cottonseed	283–297	189–198	100–115	<2
fish**	292–312	180–192	142–176	<2
groundnut (peanut)	286–300	187–196	86–107	<1
lard	276–292	192–203	45–70	<0.2
linseed	286–298	188–196	170–203	<2
olive	286–305	184–196	75–94	<1.5
palm	268–295	190–209	50–55	<1.3
palm kernel	221–244	230–254	14–21	<1
rape***	291–308	182–193	110–126	<0.2
sesame	288–300	187–195	104–120	<2
soybean	288–297	189–195	124–139	<1.5
sunflower	289–298	188–194	118–145	<2
tallow	281–295	190–200	33–47	<0.5

*SE = 56108/SV.
**Cod liver oil.
***Low erucic rape (Canola).
Data from (11).

3. HYDROLYSIS, ESTERIFICATION, AND ESTER EXCHANGE

Reactions converting acids to esters or vice versa and the exchange of ester groups are among the most widely used in fatty acid and lipid chemistry (Figure 4). They find applications from microscale preparation of methyl esters for GC analysis to the industrial production of oleochemicals and biodiesel. The exchange of groups attached to the fatty acid carboxyl is usually an equilibrium process driven to one product by an excess of one reactant or the removal of one product, and it is usually

$$\text{RCOOR}' + \text{H}_2\text{O} \rightleftharpoons \text{RCOOH} + \text{R}'\text{OH} \quad (1)$$

$$\text{RCOOH} + \text{R}'\text{OH} \rightleftharpoons \text{RCOOR}' + \text{H}_2\text{O} \quad (2)$$

$$\text{RCOOR}' + \text{R}''\text{COOH} \rightleftharpoons \text{R}''\text{COOR} + \text{RCOOH} \quad (3)$$

$$\text{RCOOR}' + \text{R}''\text{OH} \rightleftharpoons \text{RCOOR}'' + \text{R}'\text{OH} \quad (4)$$

$$\text{TAG} + \text{glycerol} \rightleftharpoons \text{MAG} + \text{DAG} \quad (5)$$

Figure 4. Exchange reactions at the carboxyl group (1) hydrolysis (Chapter xx), (2) esterification (Chapter xx), (3) acidolysis (Chapter xx), (4) alcoholysis (Chapter xx), and (5) glycerolysis (Chapter xx). The starting ester RCOOR' will often be a triacylglycerol. MAG—monoacylglycerol; DAG—diacylglycerol; TAG—triacylglycerol.

carried out with the aid of a catalyst. The catalyst may be an acid, a base, or a lipolytic enzyme. These reactions produce the fatty acids and methyl esters that are the starting point for most oleochemical production. As the primary feedstocks are oils and fats, glycerol is produced as a valuable byproduct. Reaction routes and conditions with efficient glycerol recovery are required to maximize the economics of large-scale production.

There is increasing interest in the use of lipase enzymes for large-scale reactions. Enzyme reactions require milder conditions, less solvent, and give cleaner products—attributes of "green chemistry." Enzymes can exert regio- or stereospecific control over reactions and may also offer a degree of selectivity for particular fatty acids, not observed with acid or base catalysts. Although the reactions of the carboxyl group are normally independent of those of the double bonds in the fatty acid molecule, the presence of a double bond at the $\Delta 4$, $\Delta 5$, or $\Delta 6$ position often results in slower reaction when a reaction is catalyzed by a lipase. Lipase catalyzed reactions are considered in detail below, following a brief description of the reactions involved.

3.1. Hydrolysis

The reaction can be catalyzed by acid, base, or lipase, but it also occurs as an uncatalyzed reaction between fats and water dissolved in the fat phase at suitable temperatures and pressures.

Base catalyzed hydrolysis. Historically, soaps were produced by alkaline hydrolysis of oils and fats, and this process is still referred to as saponification. Soaps are now produced by neutralization of fatty acids produced by fat splitting (see below), but alkaline hydrolysis may still be preferred for heat-sensitive fatty acids.

On a laboratory scale, alkaline hydrolysis is carried out with only a slight excess of alkali, typically 1M potassium hydroxide in 95% ethanol, refluxing for one hour, and the fatty acids recovered after acidification of the reaction mixture. This is a sufficiently mild procedure that most fatty acids, including polyunsaturates, epoxides, and cyclopropenes, are unaltered (19).

Fat splitting. The industrial production of fatty acids uses the direct reaction between water and fats, which proceeds rapidly at ~250°C and 2–6 MPa (20–60 bar). Under these conditions, water is moderately soluble in the oil phase, and stepwise hydrolysis of the triacylglycerols proceeds without the aid of a catalyst. The reaction is carried out with a countercurrent of water that removes the glycerol formed, resulting in ~99% conversion to fatty acids. Glycerol is recovered from the aqueous phase. Sonntag has reviewed industrial fat splitting in detail (20).

3.2. Esterification

Fatty acids are converted to esters by reaction with an excess of alcohol using an acid catalyst or a lipase. For the preparation of methyl esters for GC analysis, boron trifluoride, sulfuric acid, or anhydrous hydrogen chloride in methanol are commonly used (19). Reaction is complete in 30 minutes at reflux. Propyl and butyl

esters are prepared in a similar way with the corresponding alcohols. It is not always possible to use an excess of alcohol, for example, in the synthesis of triacylglycerols using a protected glycerol. A more reactive fatty acid derivative such as the acid chloride or anhydride is used, or the fatty acid is reacted directly with the alcohol, using dicyclohexylcarbodiimide (DCC) plus 4-dimethylaminopyridine (DMAP) as a coupling agent, for example, in the synthesis of acylglycerols (21). Some groups in more unusual fatty acids are acid sensitive, for example, epoxides, cyclopropanes, cyclopropenes, and hydroxy compounds, and methods avoiding acids catalysts are needed. Reaction with diazomethane or the less hazardous trimethylsilyl-diazomethane are possibilities (19).

3.3. Ester Exchange Reactions

The fatty acid or alcohol groups present in an ester can be exchanged in a number of ways: by reaction with an excess of other fatty acids (acidolysis), alcohols (alcoholysis), or other esters (interesterification). Generally, the starting point will be a triacylglycerol, and these reactions provide routes by which the composition and properties of oils and fats can be modified.

Acidolysis. This reaction can be acid or enzyme catalyzed and may be used to modify triacylglycerol composition. Acidolysis of an oil containing only C_{16} and C_{18} fatty acids with fatty acids rich in lauric acid (e.g., from palm-kernel oil) results in a triacylglycerol enriched in medium-chain fatty acids.

Alcoholysis. Methanolysis of triacylglycerols is used to prepare methyl esters for fatty acid analysis, a process frequently referred to as transesterification. This can be acid-or base-catalyzed, the method being chosen to avoid modifying acid-or base-sensitive fatty acids and to minimize reaction times. Sterol esters of fatty acids react more slowly than triacylglycerols, and samples containing them require more vigorous reaction conditions. The preparation of methyl esters from oils and fats for GC and GC-MS analysis has been extensively reviewed (19, 22, 23).

Biodiesel is produced on the industrial scale by methanolysis of vegetable oils (usually rape or soybean) or waste fat, particularly using frying oils. Methanolysis proceeds with modest amounts of base catalyst, provided the levels of free fatty acid and water in the oil are low (24, 25). The fatty acid content may be reduced by physical or chemical treatment before methanolysis but for waste fats, alternative processes that do not use base catalysis may be preferred. Lipase catalyzed methanolysis is less sensitive to fatty acid and water in the oil and has been tested in batch (26) and fixed-bed reactor (27) conversion of waste oil and grease to biodiesel.

Glycerolysis, the treatment of triacylglycerols with glycerol and a basic catalyst (sodium hydroxide or sodium methoxide), is used to produce mono- and diacylglycerols on an industrial scale. Molecular distillation is used to produce MAG, which is 90–95% pure and is widely used as an emulsifying agent in foods and other applications.

Interesterification. Interesterification is the intra- and intermolecular exchange of fatty acids on the glycerol backbone of triacylglycerols, although the term is also used more loosely to include acidolysis and other ester exchange reactions. It is applied to either an individual oil or a blend of oils, to produce triacylglycerols with different properties. The molecular species of natural triacylglycerols is not a random mixture of all possible isomers, but it shows greater or lesser selectivity in the distribution of fatty acids between the *sn*-1 and *sn*-3 and the *sn*-2 positions (Table 5). This, as well as the overall fatty acid mixture, determines many of the technically important properties of the oil or fat, for example, solid fat content and melting point. Once subjected to interesterification with a chemical catalyst, the triacylglycerol becomes a random mixture of molecular species. Lipase catalyzed interesterification may alter the distribution of molecular species in a more selective way.

Chemical interesterification (28, 29) is carried out at moderate temperatures (70–100°C), with neat oils and a low concentration (<0.4%) of a base catalyst such as sodium methoxide or ethoxide or Na/K alloy. As the catalyst is destroyed by water and free fatty acids, the oil must be carefully refined and dried before adding the catalyst. Reaction proceeds through sequential fatty acid exchange reactions, following formation of what is believed to be the true catalyst, the alkali metal derivative of a diacylglycerol. There is no observed selectivity for fatty acid or glycerol position, leading to a fully random product. The product composition can be controlled through directed interesterification at lower temperatures. Na/K alloy is used as catalyst as it is active at temperatures below 50°C and cooling the reaction mixture causes high melting trisaturated triacylglycerols to crystallize out, altering the composition of the liquid phase in which reaction occurs. The remaining liquid phase is randomized by further reaction and high melting products continue to crystallize out, eventually leading to solid and liquid products richer in trisaturated and triunsaturated species than the fully randomized fat (29).

Interesterification is used to modify fat properties without recourse to partial hydrogenation. Hardened fats produced by partial hydrogenation contain *trans*-isomers, which are now regarded as undesirable by nutritionists and will be increasingly subject to product labeling regulations. Liquid fats can be hardened by interesterification with fully saturated fats (either stearin fractions or fully hydrogenated oils), raising the solid fat content without isomerizing any of the fatty acids. The use of interesterification to produce margarine and spreads has increased recently, particularly in Europe.

3.4. Lipase Catalyzed Reactions

Lipases are enzymes that hydrolyze fatty acids from lipid species (e.g., triacylglycerols or phospholipids) in vivo. A number of lipases, mainly of bacterial origin, are now available immobilized onto a solid support for use as industrial scale catalysts.

Immobilized lipases catalyze the whole range of ester exchange reactions described above (alcoholysis, acidolysis, esterification) as well as hydrolysis. There are two significant differences between lipase and chemically catalyzed reactions. First, lipase catalyzed reactions take place at a lower temperature and with fewer side reactions, leading to cleaner products: an environmentally friendly alternative to some existing processes. Second, enzyme catalyzed reactions are more selective, offering control over reactions not possible with a chemical catalyst. Selectivity may be for fatty acids at different positions on the glycerol backbone (*sn*-1 and *sn*-3 rather than *sn*-2) or for particular fatty acids, discriminating by double-bond position or chain length (30, 31). The widely studied Lipozyme RM IM (*Rhizomucor miehei* lipase immobilized onto a weak anion exchange resin) preferentially hydrolyzes short-chain acids relative to medium and long chains from triacylglycerols. Hydrolysis at the *sn*-1 position is somewhat faster than at *sn*-3, and hydrolysis at *sn*-2 is very slow (31).

Lipase catalyzed reactions take place in the neat oil or in a nonpolar (usually hydrocarbon) solvent. The efficiency depends on the amount of water, solvent (if present), temperature, and ratio of reactants. A factorial approach can be used to optimize the conditions (32). In interesterification reactions, 1,3-specific enzymes give control over product composition that is not possible using chemical catalysts. For example, starting with SOS and OOO, chemical interesterification produces all eight possible isomers (see Table 5). Enzymatic interesterification does not exchange fatty acids at the *sn*-2 position, and it will result in only two additional molecular species, OOS and SOO. In more realistic situations, chemical and enzymatic interesterification may produce the same or a similar number of molecular species, but in different proportions (31).

Enzymatic interesterification has most potential for high-value products such as confectionary fats and nutritional products, for example, cocoa butter equivalents prepared from cheap and readily available starting materials. Acidolysis of palm mid fraction, rich in POP, with stearic acid gives a cocoa butter equivalent rich in POSt and StOSt, through exchange at the *sn*-1 and *sn*-3 positions while retaining the oleate at the *sn*-2 position. Tripalmitin treated similarly with oleic acid gives products where the palmitate is retained at the *sn*-2 position, whereas oleate is introduced at *sn*-1 and *sn*-3, producing a human milk fat substitute such as Betapol. In practice, pure starting materials are not used. Feedstocks rich in tripalmitin and oleic acid are reacted in a two step-process: alcoholysis to *sn*-2- monoacylglycerols followed by esterification (33).

Both batch and fixed-bed reactors have been used and tested on the near ton scale (34) for the production of high-value fats. This technology has now progressed to pilot production, using a 1-m^3 fixed-bed plug-in reactor containing the immobilized enzyme Lipozyme TL IM (35). Blends of palm oil or stearin with palm-kernel or coconut oil are interesterified in less than one hour at 70°C, and no downstream processing is required as the enzyme is retained in the reactor. This is a practical, lower energy alternative to hydrogenation and chemical interesterification, free from the *trans*-isomer production of the former and more selective and "natural" than the latter.

Lipases also discriminate between fatty acids with different double-bond positions. The reaction of fatty acids with Δ4, Δ5, and Δ6 double bonds is significantly slower than Δ9 acids when catalyzed by some enzymes. This is illustrated by some examples of attempts to concentrate γ-linolenic acid (GLA; 18:3 6*c*9*c*12*c*) from borage oil. Hydrolysis of borage oil with *Candida rugosa* lipase resulted in selective hydrolysis of the Δ9 acids (mainly 18:2) increasing the amount of GLA in the remaining acylglycerols (36). The efficiency of the enrichment was influenced by the initial triacylglycerol composition and the extent of hydrolysis. Starting with a borage oil containing 22% GLA, the upper limit of enrichment was to 46%, but higher values resulted from repeated hydrolysis of the recovered acylglycerols. A two-step sequence involving both enzymatic hydrolysis and re-esterification achieved higher enrichment (37). Nonselective hydrolysis with *Pseudomonas* sp. lipase was optimized for high GLA recovery (93%). Esterification with lauryl alcohol, using *Rhizopus delemar* lipase, discriminated strongly against GLA, resulting in enrichment in the unesterified fatty acids from 22.5% to 70.2% with a recovery efficiency of 75.1%. A 92.1% GLA concentrate, obtained by low-temperature crystallization of borage oil fatty acids, was enriched to 99.1% by esterification with butanol, catalyzed by Lipozyme IM-60 (38).The overall recovery was 72.8%. The operating parameters (alcohol, concentration, temperature, and solvent) were systematically investigated.

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), Δ5 and Δ4 acids respectively, are discriminated against during lipase catalyzed reactions and reaction of DHA may be significantly slower than EPA. Alcoholysis of tuna oil ethyl esters with lauryl alcohol using *Rhizomucor miehei* lipase enriches the DHA in the unreacted ethyl esters, whereas the concentration of EPA is simultaneously reduced (39). A concentrate containing 60% DHA and 8.6% EPA was alcoholyzed with excess lauryl alcohol (1:7 mole ratio). The remaining ethyl esters contained 93% DHA in 74% recovery, and EPA was reduced to 2.9%. Both nonregiospecific and *sn*-1,3-specific enzymes incorporate GLA into seal blubber and menhaden oil (3:1 mole ratio of GLA to triacylglycerol) producing an oil rich in both n-3 and n-6 polyenes (40). The highest incorporation was with the nonspecific enzyme.

4. OXIDATION

The fatty acid alkyl chain is susceptible to oxidation both at double bonds and adjacent allylic carbons. Free-radical and photooxidation at allylic carbons are responsible for deterioration of unsaturated oils and fats, resulting in rancid flavors and reduced nutritional quality, but they are also used deliberately to polymerize drying oils. Oxidation of double bonds is used in oleochemical production either to cleave the alkyl chain or to introduce additional functionality along the chain. Enzyme catalyzed oxidation is the initial step in the production of eicosanoids and jasmonates (biologically active metabolites in animals and plants respectively) but is not discussed further here.

4.1. Autoxidation and Photooxidation

Both autoxidation and photooxidation produce allylic hydroperoxides from unsaturated centers.

$$\sim\!\!\sim CH{=}CH{-}CH_2\sim\!\!\sim + O_2 \longrightarrow \sim\!\!\sim CH{=}CH{-}CH(OOH)\sim\!\!\sim$$

During this process, the position and geometry of the double bond may change. The hydroperoxide mixtures produced by autoxidation and photooxidation are not the same, indicating that different mechanisms are involved. Free radical oxidation can be promoted or inhibited. Deliberate promotion speeds the polymerization of drying oils, and strenuous efforts are made to inhibit the onset of rancidity in edible oils. Frankel has recently reviewed this topic in depth (41); see also (1) for an extensive discussion of oxidation of food lipids.

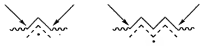
4.1.1. Autoxidation Autoxidation is a free-radical chain reaction, involving a complex series of reactions that initiate, propagate, and terminate the chain.

initiation	$RH \rightarrow R^{\bullet}$	
propagation	$R^{\bullet} + O_2 \rightarrow ROO^{\bullet}$	fast
	$ROO^{\bullet} + RH \rightarrow ROOH + R^{\bullet}$	rate determining
termination	$R^{\bullet}, ROO^{\bullet} \rightarrow$ stable products	

The chain reaction is initiated by abstraction of an allylic hydrogen to give an allylic radical stabilized by delocalization over three or more carbons. The initiator is a free radical, most probably produced by decomposition of hydroperoxides already present or produced by photooxidation. The decomposition may be thermal, but it is more likely promoted by traces of variable redox state metal ions. Autoxidation is characterized by an induction period during which the concentration of free radicals increases until the autocatalytic propagation steps become dominant. During the induction period, there is little increase in oxidation products.

The first step of the propagation sequence is reaction of the allylic radical with molecular oxygen, producing a peroxy radical. This step is much faster than the subsequent abstraction of another allylic hydrogen by the peroxy radical, producing both an allylic hydroperoxide and a new allylic radical that continues the chain reaction. Hydrogen abstraction is the rate-determining step and is therefore selective for the most readily abstracted hydrogen. Methylene-interrupted dienes and polyenes, where the allylic radical can be delocalized over five carbons, are oxidized faster than monoenes where the radical is delocalized over three carbons (Figure 5).

The chain reaction is terminated by reactions that remove radicals that would otherwise produce more allylic radicals by hydrogen abstraction. Examples are the combination of two hydroperoxy radicals leading to nonradical products and molecular oxygen or reaction with a free-radical scavenger (antioxidant) generating a more stable radical.



(a) (b)

Figure 5. Allylic radicals produced during autoxidation. (a) Those from isolated double bonds are delocalized over three carbons. (b) Those from methylene-interrupted dienes or polyenes are delocalized over five carbons. The arrows show the site of attachment of O_2 giving a peroxy radical.

The rate of autoxidation generally increases with increasing unsaturation. Linoleate, as neat methyl or ethyl ester, reacts approximately 40 times faster than oleate, and for higher polyenes, the rate doubles for each additional double bond (42). Trilinolein does not follow the same kinetics as the simple esters and oxidizes somewhat faster. The medium also influences susceptibility to oxidation, and these generalizations may not hold in emulsified systems (e.g., many food formulations) where oxidation occurs at the interface between aqueous and fat phases (43). In aqueous micelles, EPA and DHA are unexpectedly stable (44), oxidizing much more slowly than linoleate. In one experiment, over half the linoleate was oxidized within 50 hours and ~90% of EPA and DHA was still present after 2000 hours. The stability of the higher polyenes is attributed to their tightly coiled configuration in the aqueous medium, making attack by oxygen or free radicals more difficult.

Mechanistic studies of autoxidation have concentrated on methylene-interrupted fatty acids, but many of the observations are valid for other compounds. Conjugated fatty acids such as CLA also oxidize through an autocatalytic free radical reaction, with the predominant hydroperoxide determined by the geometry of the conjugated diene system (45). Other groups with activated methylenes may be susceptible to oxidation, for example, the ether methylenes of ethoxylated alcohols used as surfactants (46).

4.1.2. Photooxidation Light, in the presence of oxygen, promotes oxidation of unsaturated fatty acids. Ultraviolet radiation decomposes existing hydroperoxides, peroxides, and carbonyl and other oxygen-containing compounds, producing radicals that initiate autoxidation (42). Photooxidation by longer wavelength near ultraviolet or visible light requires a sensitizer. Naturally present pigments such as chlorophyll, hematoporphyrins, and riboflavin act as sensitizers as do dyes, including erythrosine and methylene blue. Light excites these sensitizers to the triplet state that promotes oxidation by type I and type II mechanisms. Unlike autoxidation, there is no induction period.

In type I photosensitized oxidation, the triplet state sensitizer abstracts a hydrogen or electron from the unsaturated oil, producing radicals that initiate chain propagation as in autoxidation. However, chain-breaking antioxidants do not stop this reaction as new radicals are produced photochemically. In type II photooxidation, the energy of the triplet sensitizer is transferred to molecular oxygen, converting it

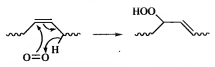


Figure 6. Ene reaction between singlet oxygen and an olefinic bond. The hydroperoxide may be attached to either of the inital double bond carbons.

to its excited singlet state. Singlet oxygen is highly electrophilic and reacts rapidly with olefins in an ene reaction, producing allylic hydroperoxides with oxygen attached to one of the original olefinic carbons and the shifted double bond now *trans* (Figure 6).

The ene reaction differs from free-radical oxidation, where oxygen attaches to an outer carbon of the delocalized allylic radical (Figure 5), resulting in a different mixture of hydroperoxides. For example, photooxidation of linoleate produces four isomers: 9-OOH,10*t*12*c*, 10-OOH,8*t*12*c*, 12-OOH,9*c*13*t*, and 13-OOH,9*c*11*t*. The same 9- and 13-hydroperoxides are produces by autoxidation, but the 10- and 12-hydroperoxides are only produced by photooxidation.

Photooxidation is much faster than autoxidation; the reaction of linoleate with singlet oxygen is approximately 1500 times faster than that with triplet oxygen (47). There is less difference in the rate of photooxidation between monoenes and polyenes than is seen in autoxidation. The relative rates for oleate, linoleate, linolenate, and arachidonate are 1.0, 1.7, 2.6, and 3.1 (48, 49). This contrasts with the 40-fold increase in rate of autoxidation between oleate and linoleate.

4.1.3. Decomposition of Hydroperoxides Allylic hydroperoxides are reactive molecules and decompose readily in a complex series of reactions, the course of which depends on the medium and other conditions (1, 41). Cleavage between the oxygens is energetically favored, leading to alkoxy and hydroxyl radicals. Redox metal ions such as Fe^{2+}/Fe^{3+} and Cu^{+}/Cu^{2+} are particularly effective catalysts. The resulting radicals can initiate further autoxidation and produce a number of stable products, many with undesirable nutritional and flavor properties (Figure 7). Products with the same chain length as the alkoxy radical include epoxides, ketones, and hydroxy fatty acids. The significant products producing off-flavors are those resulting from chain scission β to the alkoxy radical, producing shorter chain aldehydes and hydrocarbons. Alkadienals have particularly low-odor thresholds and a few parts per billion of nonadienals from n-3 fatty acids are responsible for a marked fishy taint even when other signs of oxidation are absent (50).

There are a number of analytical measures of oxidative deterioration of oils and fats. The most widely used are the peroxide value (PV) (15), which measures the hydroperoxide content by iodine titration and the anisidine value (AV) (15), which detects aldehydes by a color reaction. As an oil suffers damage because of autoxidation, the hydroperoxide content, and PV rise but do not do so indefinitely. As the hydroperoxides break down, the concentration of aldehydes and AV increase. Oxidation is better assessed by a combination of PV and AV, the Totox value

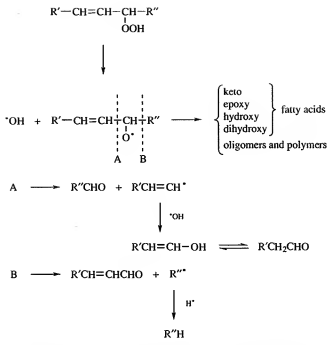


Figure 7. Decomposition reactions of allylic hydroperoxides.

(= 2 × PV + AV) being a better index of oxidation than either PV or AV alone. Volatile products can be removed from oils by deodorization, but aldehydes attached to the carboxyl end of the chain remain part of the triacylglycerol (sometimes called "core" aldehydes) and are indicators of previous oxidative damage.

4.1.4. Antioxidants Lipid oxidation is influenced by many factors: the medium, oxygen concentration, temperature, light, degree of unsaturation, and metal ions among others. In the presence of oxygen, oxidation cannot be entirely prevented nor can it be reversed, but it can be inhibited, delaying the buildup of oxidized products to unacceptable levels. Antioxidants can interact with several steps of free-radical or photooxidation. Their performance is medium and concentration dependent and requires care as they can also act as prooxidants under some conditions (51).

The most widely used antioxidants are free radical scavengers that remove reactive radicals formed in the initiation and propagation steps of autoxidation. A number of natural or synthetic phenols can compete, even at low concentrations, with lipid molecules as hydrogen donors to hydroperoxy and alkoxy radicals, producing hydroperoxides and alcohols and an unreactive radical. β-carotene reacts with peroxy radicals, producing a less-reactive radical. These stabilized radicals do not initiate or propagate the chain reaction.

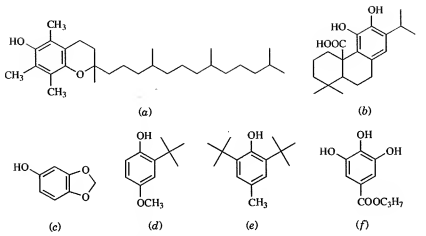


Figure 8. *Natural antioxidants (a) α-tocopherol, (b) carnosic acid, and (c) sesamol. Synthetic antioxidants (d) butylated hydroxyanisole (BHA), (e) butylated hydroxytoluene (BHT), and (f) propyl gallate.*

Tocopherols are phenolic antioxidants (Figure 8) naturally present in most plant oils (see Chapter X). They are concentrated in the distillate from physical refining, which results in a corresponding decrease in the refined oil. Soybean distillate is a source of tocopherols for antioxidant formulations. Carnosic acid (Figure 8) is isolated from rosemary and other herbs. Sesamol (Figure 8) is a characteristic antioxidant of sesame oil, responsible for its high stability (Chapter xx). Synthetic antioxidants are monocyclic phenols with highly branched substituents (Figure 8). In all of these compounds, the radicals formed by abstraction of the phenolic hydrogen are highly delocalized and unreactive. The antioxidant action of free-radical scavengers is sacrificial, delaying oxidation until the antioxidant is used up. Oxidized tocopherols may be regenerated by ascorbic acid, extending their effective life while keeping their concentration below prooxidant levels.

Photooxidation is not inhibited by free-radical scavengers. Natural pigments that act as sensitizers may be reduced during refining, increasing stability. Singlet oxygen and excited state sensitizers can be deactivated either by competitive reaction or physical energy transfer, for example, to β-carotene. Tocopherols and some amines also act as singlet oxygen quenchers through physical energy transfer.

Redox metal ions, particularly iron and copper, react with hydroperoxides, initiating further autoxidation and producing undesirable decomposition products. Complete removal of these metal ions is not possible, but steps can be taken to reduce their effect. Chelating agents such as EDTA, citric acid, phosphate, and polyphosphates may reduce the effective metal ion concentration. Their efficacy depends on pH, and they may also show prooxidant activity. The role of metal ions in hydroperoxide decomposition in food emulsions has been reviewed recently (52).

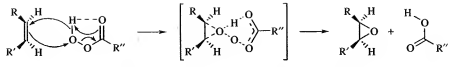


Figure 9. Epoxidation mechanism proposed by Bartlett (53). The cis-olefin gives rise to a cis-epoxide.

4.2. Epoxidation

Epoxides are produced by reaction of double bonds with peracids. This proceeds by a concerted mechanism, giving *cis* stereospecific addition (Figure 9) (53). Thus, a *cis* olefin leads to a *cis* epoxide and a *trans* olefin to a *trans* epoxide. The order of reactivity of some peracids is *m*-chloroperbenzoic > performic > perbenzoic > peracetic; electron withdrawing groups promote the reaction. The carboxylic acid produced is a stronger acid than the strongly hydrogen bonded peracid and may lead to subsequent ring opening reactions especially in the case of formic acid. Small scale reactions are carried out with *m*-chloroperbenzoic acid in a halocarbon or aromatic solvent, in the presence of bicarbonate to neutralize the carboxylic acid as it is formed (54, 55).

Oils, mainly soybean but also linseed, are epoxidized on an industrial scale (100,000 tons per year) as stabilizers and plasticizers for PVC. The reactive epoxide groups scavenge HCl produced by degradation of the polymer. Epoxidation is carried out with performic or peracetic acid produced in situ from formic or acetic acid and high strength hydrogen peroxide (70% w/w). Peracids are unstable, and the reaction is exothermic. The concentration of peracid is kept low by using a low concentration of the carboxylic acid either in the neat oil or in a hydrocarbon solvent. The carboxylic acid is regenerated after epoxidation. Complete epoxidation is not achieved as in the acidic medium ring opening reactions occur producing dihydroxy and hydroxy carboxylates as byproducts.

Recent studies have attempted to improve the efficiency of epoxidation under milder conditions that minimize the formation of byproducts. Chemo-enzymatic epoxidation uses the immobilized lipase from *Candida antartica* (Novozym 435) (56) to catalyze conversion of fatty acids to peracids with 60% hydrogen peroxide. The fatty acid is then self-epoxidized in an intermolecular reaction. The lipase is remarkably stable under the reaction conditions and can be recovered and reused 15 times without loss of activity. Competitive lipolysis of triacylglycerols is inhibited by small amounts of fatty acid, allowing the reaction to be carried out on intact oils (57). Rapeseed oil with 5% of rapeseed fatty acids was converted to epoxidized rapeseed oil in 91% yield with no hydroxy byproducts. Linseed oil was epoxidized in 80% yield. Methyl esters are also epoxidized without hydrolysis under these conditions.

Methyltrioxorhenium (MTO) catalyses direct epoxidation by hydrogen peroxide. The reaction is carried out in pyridine, avoiding acidic conditions detrimental to high epoxide yield and uses less concentrated hydrogen peroxide (30%) than other methods (58). This method epoxidized soybean and metathesized (see Section 7.4)

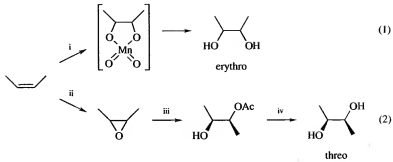


Figure 10. Stereochemistry of hydroxylation reactions: (1) with dilute alkaline permanganate and (2) through epoxide ring opening. (i) $KMnO_4$, NaOH; (ii) m-chloroperbenzoic acid, $NaHCO_3$, CH_2Cl_2; (iii) CH_3COOH; (iv) base catalyzed hydrolysis.

soybean oil in high yield (59). The epoxidized metathesized oil was more stable to polymerization than that produced using *m*-chloroperbenzoic acid, presumably because it was free of acidic impurities. These and other novel approaches to epoxidation have recently been reviewed (4, 60, 61). None has yet found industrial application.

Epoxides are reactive and readily ring open in acid, following protonation of the epoxy oxygen (Figure 10). This is a route to diols (see Section 4.3), polyols used in polymer production and a range of α-hydroxy compounds. Ring opening of methylene-interrupted diepoxides leads to 5 and 6 membered ring ethers through neighboring group participation (7).

4.3. Hydroxylation

Double bonds are converted to monohydroxy derivatives by acid catalyzed addition of carboxylic acids, followed by hydrolysis. The carbocation intermediate is prone to rearrangement, leading to a mixture of positional isomers. Hydroboration with borane:1,4-oxathiane followed by alkaline hydrolysis a regioselective reaction (62) has been used to prepare hydroxy fatty acids as GC-MS standards in high yield (63).

Hydroxylation reactions leading to diols have much in common with epoxidation and oxidative cleavage reactions (see Section 4.4), the end product depending on the strength of the oxidizing agent. Dilute alkaline permanganate or osmium tetroxide react through cyclic intermediates resulting from *cis* addition of the reagent giving an *erythro* diol. Ring opening epoxides with acid is a *trans* addition, leading to a *threo* product (Figure 10).

An oxygen bridged manganese complex was recently reported to catalyze double-bond oxidation by hydrogen peroxide leading to a mixture of epoxide, *cis*-diol, and hydroxy ketone products (64). This is an interesting model reaction for the efficient use of hydrogen peroxide as a cheap hydroxylating agent if the selectivity can be improved. A number of microorganisms are reported to produce

a range of novel di- and trihydroxy fatty acids and are being investigated as potential biocatalysts (65).

4.4. Oxidative Cleavage

Double bonds are cleaved by a number of oxidizing agents, converting the olefinic carbons to carboxylic acids, aldehydes, or alcohols. Fatty acids give a monofunctional product from the methyl end and a difunctional product from the carboxyl end (along with low-molecular-weight products from methylene-interrupted systems).

Although now largely superceded by GC and GC-MS methods for structure determination, oxidative cleavage with ozone or permanganate/periodate and identification of the resulting products is a powerful method for double-bond location, particularly for monoenes (19). Reaction with alkaline permanganate/periodate proceeds through the diol resulting from reaction with dilute permanganate (see Section 4.3). The diol is split into two aldehydes by reaction with periodate, and the aldehydes are subsequently oxidized to carboxylic acids by permanganate. Alternatively, diols derived from double bonds are cleaved to aldehydes by lead tetraacetate or periodate.

Ozone reacts directly with double bonds under mild conditions and is the preferred degradative method for double-bond location (19). The reaction occurs in several steps (64), starting with a 1,3-dipolar cycloaddition (Figure 11). The addition product decomposes rapidly into an aldehyde and a carbonyl oxide. In the absence of solvent or in nonparticipating solvents, these recombine forming a relatively stable 1,2,4-trioxolane or ozonide. The separation into aldehyde and carbonyl oxide during this rearrangement is supported by production of six ozonide species from unsymmetrical olefins. Ozonides can be converted to a number of stable products; oxidation yields carboxylic acids, mild reduction gives aldehydes, and treatment with nickel and ammonia gives amines providing useful synthetic routes to difunctional compounds from fatty acids [e.g., Furniss et al. (67)]. In a carboxylic acid or alcohol solvent, the carbonyl oxide reacts with the solvent producing mainly

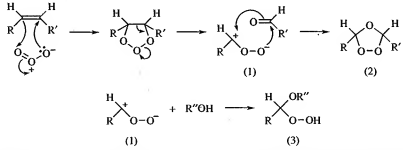


Figure 11. Ozonolysis reaction mechanism. In nonparticipating solvents, the carbonyl oxide (1) and aldehyde recombine to give the moderately stable ozonide (2). Hydroperoxides (3) are formed in protic solvents, and R″ can be alkyl or acyl.

acyloxy or alkoxyhydroperoxides, respectively, along with other more complex products (68). These hydroperoxides are oxidized or reduced to the same products as the ozonides.

Ozonolysis is the only oxidative cleavage that is used industrially. Around 10,000 tons per year of azelaic acid (nonane-1,9-dioic acid) are produced along with pelargonic acid (nonanoic acid) by ozonolysis of oleic acid. Azelaic acid is used for polymer production and is not readily available from petrochemical sources. Other dibasic acids potentially available by this route are brassylic (tridecane-1,13-dioc) and adipic (hexane-1,6-dioic) acids from erucic (22:1 13*c*) and petroselenic (18:1 6*c*) acids, respectively. High-purity monoenes are required as feedstock to avoid excessive ozone consumption and byproducts. Ozonolysis is a clean reaction, carried out at low temperatures without catalyst. However, ozone is toxic and unstable, as are the intermediates. Industrial scale ozonolysis is carried out in pelargonic acid run countercurrent to ozone at 25–45°C followed by decomposition at 60–100°C in excess oxygen (69). Ozone must be generated continuously on-site by electrical discharge in air, and ozone production is the limiting factor for large-scale production (70).

Ruthenium oxide (RuO_4) catalyzes oxidative cleavage of oleic acid to pelargonic and azelaic acids efficiently in the presence of NaOCl as an oxygen donor to regenerate Ru(VIII) (71). However, the production of halogen salt byproducts makes this impractical for large-scale production. Hydrogen peroxide and peracetic acid are cheaper and more environmentally benign oxidants, the byproduct from reaction or regeneration of peracid being water, but give very low yields with RuO_4. Ruthenium(III) acetylacetonate ($Ru(acac)_3$) with peracetic acid or Re_2O_7 with hydrogen peroxide give moderate yields with internal double bonds, but ~80% conversion with terminal olefins. Terminal olefins, produced from fatty acids with an internal double bond by metathesis with ethylene, are converted to dibasic acids without

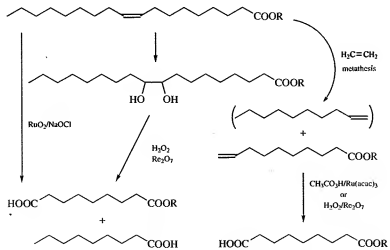


Figure 12. *Alternative oxidative cleavage reactions.*

concomitant production of monobasic acids. Diols produced by hydroxylation are cleaved by Re_2O_7 with hydrogen peroxide to di- and monobasic acids (Figure 12). These reactions offer an alternative to ozonolysis for the production of dibasic acids, but they have still to be optimized for industrial application (71, 72).

5. REDUCTION

Both carbon–carbon double bonds and the carboxyl group of fatty acids can be reduced, either together or separately depending on the reaction conditions. Catalytic reduction is an important industrial route to hardened fats, fatty alcohols, and fatty amines, using well-established technologies.

5.1. Hydrogenation of Double Bonds

Transition metals such as Co, Ni, Cu, Ru, Pd, and Pt catalyze hydrogenation of double bonds. Palladium on charcoal or Adam's catalyst (platinum oxide) promote saturation of fatty acids at ambient temperature and hydrogen pressure. Hydrogenation is accompanied by exchange and movement of hydrogen atoms along the chain in the region of the double bonds, demonstrated by the large number of isotopomers formed on deuteration. Homogeneous deuteration with Wilkinson's catalyst (tris (triphenylphosphine)rhodium(I) chloride) proceeds without hydrogen movement or exchange (73) and in conjunction with GC-MS analysis is used to locate double bonds. Partial hydrogenation with hydrazine does not isomerize unreacted double bonds and is useful for structural analysis of polyenes and was recently used to examine long-chain metabolites of conjugated linoleic acid (CLA) (74).

5.2. Catalytic Partial Hydrogenation

Partial hydrogenation reduces the polyene content of oils while maintaining or increasing the monoene content. Reduction of double bonds is accompanied by a variable degree of *cis*-to *trans*-isomerization. "Brush" hydrogenation of soybean or rape oil reduces linolenic content, improving oxidative stability, whereas more extensive hydrogenation increases solid fat content, producing "hardened" fats for spreads and shortenings. Partial hydrogenation has been used for the past century, in margarine production and remains an important process for edible fat modification (Chapter xx) despite concerns about adverse nutritional properties of *trans*-fatty acids. There are recent reviews of the mechanism (75, 76) and technology (77).

A number of uncertainties remain about the mechanism of the reaction and the factors controlling selectivity between polyenes and monoenes, and the balance between hydrogenation and isomerization. Hydrogenation is a three-phase reaction among liquid oil, gaseous hydrogen, and solid catalysts carried out as a batch process in autoclaves to maintain consistent products. Temperature, hydrogen pressure, amount and formulation of catalyst, and agitation are all carefully controlled.

Supported nickel is invariably used as catalyst. Although other catalysts are equally or more effective, nickel has widespread acceptance from long use, ease of removal, and low cost. Unremoved traces of other metals such as copper might also reduce the oxidative stability of the product.

The reaction mechanism must account for the selectivity of the reaction (polyenes reacting faster than monoenes) and the production of *trans*-monoenes. Hydrogen addition is in two steps with a semihydrogenated intermediate. Addition of the first hydrogen is reversible, regenerating a double bond with potentially altered position or geometry. Addition of a second hydrogen irreversibly produces a saturated bond (Figure 13). Dijkstra (76) proposed that for dienes, the formation of the semihydrogenated intermediate is rate determining and hydrogen concentration dependent, whereas for the conversion of monoene to saturate, the rate-determining and hydrogen concentration-dependent step is the addition of the second hydrogen. At low dissolved hydrogen concentrations, isomerization of monoenes is favored over saturation, allowing control of the product composition by hydrogen pressure, agitation, and reaction time.

Copper catalysts show different selectivity compared with nickel. Copper only catalyzes hydrogenation of methylene-interrupted systems, showing high selectivity for polyenes and no reaction with oleate or other monoenes produced by reduction of polyenes. The first step is production of conjugated dienes that are the species hydrogenated. Dijkstra recently reassessed this reaction, suggesting removal of an allylic hydrogen as the first step in production of the conjugated diene (78).

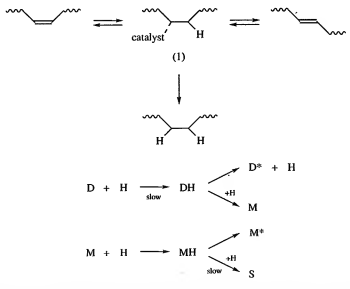


Figure 13. Partial hydrogenation. The partially hydrogenated intermediate (1) may lead to cis or trans unsaturated or saturated products. D—diene; M—monoene; S—saturate; potentially isomerized. Formation of M* is favored at a low hydrogen concentration.*

5.3. Production of Fatty Alcohols

Triacylglycerols, fatty acids, and esters can be reduced to aldehydes, alcohols, or hydrocarbons, the main application being the production of fatty alcohols. On a small scale, lithium aluminum hydride (in excess of stochiometric requirement) is a convenient reducing agent for the carboxyl group without affecting polyunsaturated chains. Industrially, catalytic hydrogenation is used and has been reviewed (79, 80).

Long-chain alcohols are produced from both oleochemical and petrochemical sources. Oils and fats provide straight chain lengths not readily available otherwise and the possibility of unsaturated chains. The main feed stocks are coconut and palm-kernel oil for C_{12}–C_{14} alcohols and technical grades of tallow and palm oil for C_{16}–C_{18} alcohols. The preferred starting material for catalytic hydrogenation is methyl ester. Fatty acids are corrosive and need harsh reaction conditions, leading to unwanted byproducts. Reduction of intact oils leads to loss of glycerol, a valuable byproduct, through over-reduction to propane diol and propanol, as well as excessive hydrogen and catalyst consumption. Methyl esters are reduced to saturated alcohols with copper chromite catalyst (~2%) at 250–300°C and 25–30-MPa (250–300 bar) hydrogen in a suspension system or at 200–250°C with a fixed-bed catalyst. The methanol produced is recycled for methyl ester production. Zinc-based catalysts do not hydrogenate double bonds and are used to produce unsaturated alcohols such as oleyl alcohol.

6. PRODUCTION OF SURFACE ACTIVE COMPOUNDS AND OLEOCHEMICALS

The main non-food use of oils and fats is the production of surfactants. The amphiphilic properties of fatty acids, exploited for centuries in the use of soaps, can be modified by changing the carboxyl group into other hydrophilic groupings, giving anionic, cationic, amphoteric, and nonionic surfactants. There is also scope for functionalizing the aliphatic chain, but this has not been widely used commercially. The chain length of the feed stock, C_{12}–C_{14} from lauric oils, C_{22} from high erucic rape and fish oils, and C_{16}–C_{18} from most other sources, can be used to modify solubility. The main starting materials for surfactant production are fatty acids and alcohols with a range of N-containing derivatives produced through amides and amines. Surfactants of oleochemical origin may biodegrade better than petrochemical products, giving an environmental benefit in addition to being derived from renewable resources. Recently, surfactants have been produced from fully renewable resources. Oleochemical surfactant production has been reviewed (81–85).

6.1. Nitrogen-Containing Compounds

The presence of nitrogen, either in a neutral or cationic group, gives surfactant properties that are not easily produced with other compounds. A diverse range of nitrogen-containing compounds are produced, for which the starting point is an

TABLE 7. Routes to Nitrogen-Containing Surfactants.

	Product
$RCH_2NH_2 + CH_2O \rightarrow$ (reduction) $\rightarrow RCH_2NMe_2$	tertiary amine
$RCH_2CONMe_2 \rightarrow$ (reduction) $\rightarrow RCH_2NMe_2$	tertiary amine
$RCH_2OH + Me_2NH \rightarrow$ (catalytic hydrogenation) $\rightarrow RCH_2NMe_2$	tertiary amine
$ROH + CH_2{=}CHCN \rightarrow RO(CH_2)_2CN \rightarrow$ (reduction) $\rightarrow RO(CH_2)_3NH_2$	etheramine
$RNH_2 + CH_2{=}CHCN \rightarrow RNH(CH_2)_2CN \rightarrow$ (reduction) $\rightarrow RNH(CH_2)_3NH_2$	diamine
$RNH(CH_2)_3NH_2 + CH_2{=}CHCN \rightarrow RNH(CH_2)_3NH(CH_2)_2CN \rightarrow$ (reduction) $\rightarrow RNH(CH_2)_3NH(CH_2)_3NH_2$	triamine
$RO(CH_2)_3NH_2 + 2nCH_2(O)CH_2 \rightarrow RO(CH_2)_3N((CH_2CH_2O)_nH)_2$	ethoxylated etheramine
$RNH(CH_2)_3NH_2 + 2nCH_2(O)CH_2 \rightarrow RNH(CH_2)_3N(CH_2CH_2O)_nH)_2$	ethoxylated diamine
$RNH_2 + nCH_2(O)CH_2 \rightarrow H(OCH_2CH_2)_nN(R)(CH_2CH_2O)_nH$	ethoxylated amine
$RN(Me)_2 + (H_2O_2) \rightarrow RN^+(Me)_2O^-$	amine oxide
$RN(Me)_2 +$ (MeCl or Me_2SO_4) $\rightarrow RN^+(Me)_3\ X^-$	quaternary amine
$R_3N +$ (benzyl chloride) $\rightarrow R_3N^+Bz\ X^-$	quaternary amine
$RCOOH + NH_2(CH_2)_2NH(CH_2)_2NH_2 \rightarrow$ 4	imidazoline
$2RCOOH + (HOCH_2CH_2)_2NCH_3 \rightarrow (RCOOCH_2CH_2)_2NCH_3 + H_2O$	ester amine

amide or amine. Amides are formed by direct reaction of the fatty acid and ammonia at 180–200°C and 0.3–0.7 MPa (3–7 bar), through dehydration of the initially formed salt. Long-chain amides, e.g., erucamide, are the principle industrial products, used as polythene film additives.

Amines are produced from fatty acids in a reaction sequence in which the nitrile is an intermediate. Nitriles are produced by reaction of the fatty acid with ammonia, giving the amide that is dehydrated in situ at 280–360°C in the liquid phase on a zinc oxide, manganese acetate, or alumina catalyst. Lower temperature and longer reaction times are used with unsaturated fatty acids to avoid polymerization. Hydrogenation with nickel or cobalt catalyst reduces the nitrile to amines via the aldimine (RCH=NH). Depending on the reaction conditions, the aldimine reacts with hydrogen or primary or secondary amines, giving primary, secondary, or tertiary amines, respectively, as the major product. Primary amines are produced at 120–180°C and 2–4 MPa (20–40 bar); higher temperature and lower pressure favors production of secondary and tertiary amines with a symmetrical substitution at the nitrogen. The long-chain composition closely reflects the fatty acid composition of the feedstock, although hydrogenation conditions can be adjusted to hydrogenate the alkyl chains or induce *cis–trans*-isomerism. The more widely used unsymmetrical tertiary amines are produced from primary amines, amides, or alcohols (Table 7). Reactions converting amines to other surface-active derivatives and for the preparation of other nitrogen-containing compounds are shown in Table 7. These have appeared in several reviews (2, 82, 84, 86, 87).

6.2. Ethoxylation

Long-chain molecules with active hydrogen (alcohols, amines, and amides) react as nucleophiles with ethylene oxide usually with a basic catalyst. The product has a hydroxyl group that can react with further ethylene oxide, leading to polyoxyethylene products with a range of molecular weights. The average number of ethylene oxide molecules added depends on the reaction conditions and can be adjusted to alter the solubility and surfactant properties of the product.

$$ROH + nC_2H_4O \rightarrow RO(C_2H_4O)_nH$$

Typical reaction conditions are 120–200°C and pressures of 0.2–0.8 MPa (2–8 bar) with potassium hydroxide or sodium alcoholates as catalyst (83). In the reaction with primary amines, both active hydrogens are replaced before further ethylene oxide addition leading to dipolyoxyethylene derivatives. Polyoxyethylenes have a terminal hydroxyl that may be further functionalized under conditions that do not damage the ether linkages, for example, sulfation.

6.3. Sulfation

Sulfate esters of alcohols or polyoxyethylene alcohols are prepared by reaction with sulfur trioxide in continuous falling-film plants, immediately followed by neutralization with sodium hydroxide to give the sodium salt (81).

$$ROH + SO_3 \rightarrow ROSO_3H$$
$$ROSO_3H + NaOH \rightarrow ROSO_3Na + H_2O$$

Alcohol sulfates are not stable in acid and are used in alkaline formulations. C_{12}–C_{16} alcohol sulfates have excellent detergency, high foam, and good wetting properties. Alcohol sulfates are fully biodegradable under aerobic and anaerobic conditions and compete in performance with petrochemical-derived linear alkylbenzene sulfonates (LABS).

Mono- and diacylglycerols are starting materials for sulfate ester surfactants that can be prepared directly from triacylglycerols without reduction to the fatty alcohol. Cocomonoacylglycerol sulfates, used in cosmetic formulations, are produced in a solvent-free process (88). Glycerolysis of coconut oil (mole ratio of glycerol to oil of 2:1) gives the raw material for sulfatization, predominantly mono- and diacylglycerols. Membrane filtration is used to desalt the product.

6.4. α-Sulfonates

The methylene adjacent to the carboxyl group is sufficiently activated to react with sulfur trioxide, giving α-sulfonate products. As allylic methylenes are similarly activated, the reaction is usually carried out with saturated starting materials. The complex reaction involves two moles of sulfur trioxide, giving a disulfonate intermediate that reacts with methyl ester to give the α-sulfonate ester, or on treatment

with sodium hydroxide the disodium salt (81). α-Sulfonates have low toxicity and are fully biodegradable.

$$RCH_2COOCH_3 + 2SO_3 \rightarrow RCH(SO_3H)COOSO_2OCH_3$$

$$RCH(SO_3H)COOSO_2OCH_3 + RCH_2COOCH_3 \rightarrow 2RCH(SO_3H)COOCH_3$$

6.5. Carbohydrate-Based Surfactants

Carbohydrates and related polyols (as well as amino acids) have attracted attention as the hydrophilic component of nonionic surfactants, particularly as a benign alternative to manufacture using ethylene oxide. Sucrose, glucose, and sorbitol (from hydrogenation of glucose) are available in quantity from renewable resources. Although sorbitol esters have been in use for many years, large-scale synthesis of sugar esters remains difficult because of the similar reactivity of all the carbohydrate hydroxyls, leading to many molecular species in the product. Further difficulties are the insolubility and charring of the carbohydrate in the reaction medium. A more controllable reaction is that between long-chain alcohols and glucose, giving alkyl polyglycosides with the fatty alcohol ether linked only to position C-1 on the glucose ring. Further glucose units are also joined through ether links. Both the alcohol and glucose can be produced from renewable resources (oils and fats and starch, respectively), and the reaction can be carried out in a solvent-free system. In commercial production, glucose is suspended in excess alcohol and reacted at 100–120°C with a sulfonic acid catalyst. The product has an average degree of polymerization of 1.2 to 1.7 glucose units per molecule (Figure 14) and is nonirritant and fully biodegradable (88–91). Alkyl polyglycoside production is currently ~100,000 tons per year, which is used in detergent formulations in place of petrochemical-derived products.

6.6. Dimers and Estolides

A number of different dimers and oligomers are produced from fatty acids and alcohols. These are branched-chain compounds with significantly lower melting points than straight chain structures of similar molecular weight. Fully saturated dimers

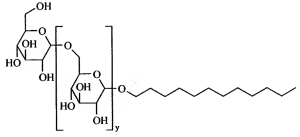


Figure 14. Alkyl polyglycoside. Degree of polymerization = y + 1.

have excellent oxidative stability. This and their extended liquid range are exploited in their use as lubricants and cosmetic additives. Polyfunctional dimers are used in polymer formulations.

Dimer acids. Dimer acids are produced by heating monoene or diene fatty acids (e.g., tall oil acids, a byproduct of wood pulping) with a cationic clay catalyst (92). Typical conditions are 4% montmorillonite at 230°C for 4–8 hours. After distillation, the product is a complex mixture of acyclic, cyclic, and bicyclic dimers along with some trimer. Dimer acids are dibasic and react with diamines and triamines to give polyamides. Imidazole derivatives are used as corrosion inhibitors and esters as lubricants.

Guerbet compounds. Guerbet alcohols have been known for over a century and are produced by the alkali catalyzed dimerization of aliphatic alcohols with accompanying loss of water. Typical reaction conditions are heating at 200–300°C with potassium hydroxide in the presence of transition metal compounds to catalyze the intermediate reduction step. Dehydrogenation of the alcohol to the aldehyde is followed by aldol condensation and rehydrogenation to give the branched-chain alcohol (Figure 15a).

The alcohols can be oxidized to the corresponding acids. Guerbet alcohols, acids, their esters, sulfates, and ether sulfates are used as lubricants, cosmetic additives, and surfactants. Their synthesis, characterization, and applications have been reviewed (93).

Estolides. Estolides are ester-linked branched-chain compounds. They are normally produced under harsh conditions similar to those used to produce dimer acids, but with the addition of around 10% water. Mono- and polyestolides are used as lubricants, greases, and surfactants, and in cosmetic, ink, and plastic formulations. Estolides biodegrade rapidly and completely, at rates comparable with the vegetable oils and fatty acids from which they are derived (94), making them environmentally benign products. The Δ5 monoene acids in meadowfoam oil form estolides under

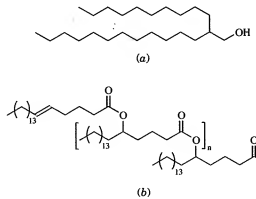


Figure 15. (a) Guerbet alcohol from lauryl alcohol (12:0). (b) Estolide from meadowfoam acids (20:1 5c).

mild acid catalysis, neighboring group participation by the carboxyl group facilitating the reaction (Figure 15b) (95). The product from meadowfoam acids shows higher regioselectivity than that from acids with mid-chain olefins where the double bond is further from the carboxyl group. Estolides from mid-chain olefins have significantly lower pour points than the corresponding fatty acids or triacylglycerols, but those from meadowfoam acids show little difference.

7. MODIFYING FATTY ACID STRUCTURE

Isomerization and conjugation change the properties of natural methylene-interrupted fatty acids, leading to new applications and potential added value. Chain shortening or extension produces fatty acids not readily isolated from natural sources and is also used to introduce radioactive or stable isotope labels. Metathesis provides a flexible method for modifying the alkyl chain.

7.1. Isomerization

Trans-isomers of fatty acids are more stable thermodynamically than *cis*-isomers, because of reduced steric crowding; the equilibrium ratio is approximately 4:1 *trans*:*cis*. There is a considerable energy barrier to interconversion (~125 kJ/mole). Before the attached groups can rotate about the double bond, it has to be weakened by coordination to a catalyst, high temperature, or temporary conversion to a single bond through addition and elimination reactions. Chemical isomerization agents leading to an equilibrium mixture include selenium (through a π-complex) and nitrogen oxides or thiols (through free-radical addition/elimination).

Cis-to *trans*-isomerization accompanies partial hydrogenation (see Section 5.2) and may be exploited to raise the melting point. Unwanted isomerization occurs during physical refining at temperatures above 250°C. More unsaturated acids isomerize faster, making linolenic containing seed oils (e.g., soybean and canola) particularly vulnerable. Conditions for deodorizing rape oil without isomerization have been optimized following a detailed study and development of a model of the isomerization kinetics (96).

7.2. Conjugation

Heating with alkali has long been used to produce conjugated drying oils for paints and varnishes. The anion resulting from removal of a bis-allylic methylene rearranges through migration and isomerization, giving a *cis,trans*-conjugated system (Figure 16). Thus, linoleic acid (18:2 9*c*12*c*) gives both 9*c*11*t* and 10*t*12*c* isomers, whereas trienes give a mixture of partially and fully conjugated isomers depending on whether the middle or an outer double bond migrates first. Under the harsh conditions used to prepare drying oils (aqueous alkali at ~230°C), a complex mixture of isomers is eventually formed, but under controlled conditions (e.g., KOH in

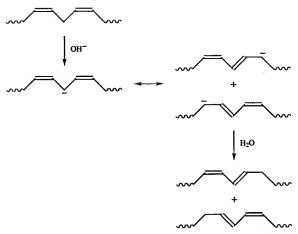


Figure 16. Alkali-induced conjugation of methylene-interrupted olefins.

propylene glycol at 150°C), a mixture containing only the 9c11*t* and 10t12*c* CLA isomers is produced (97). This product and individual isomers prepared from the mixture are used as nutritional supplements.

Thermal isomerization of linoleic acid produces a conjugated isomer mixture that does not contain all possible *cis*-and *trans*-isomers. The absence of the 8c10*t* and 11t13*c* isomers suggests a concerted pericyclic mechanism that limits the geometrical possibilities for the rearranged double bonds (98). $[RhCl(C_8H_{14})_2]_2$ in the presence of $(p\text{-}CH_3C_6H_4)_3P$ and $SnCl_2.2H_2O$ is an efficient homogeneous catalyst for the conjugation of linoleic acid, producing conjugated soybean oil with exceptional drying properties and high solvent resistance in high yield (99).

7.3 Chain Shortening and Extension

Fatty acids can be labeled at the carboxyl carbon with ^{13}C or ^{14}C by chain shortening followed by chain extension with labeled carbon. Chain shortening to the norhalide using the Hunsdieker reaction (decarboxylation of fatty acid silver salts in the presence of halogens) is only suitable for saturated acids, but unsaturation is not altered using the alternative developed by Barton employing *N*-hydroxy-pyridine-2-thione in a halocarbon solvent (100). Chain extension with labeled cyanide followed by hydrolysis or reaction of the derived Grignard reagent with labeled carbon dioxide gives the labeled fatty acid. The Barton decarboxylation was recently used to prepare gram quantities of 1-[^{13}C]-linoleic and 1-[^{13}C]-linolenic acids for metabolic studies (101).

Two-carbon chain extension at the carboxyl end, mimicking biosynthesis, uses the malonic ester route (102). After reduction of the carboxyl to an alcohol, the readily displaced mesylate is prepared and reacted with sodium diethylmalonate. Saponification and decarboxylation gives the chain extended product in high yield.

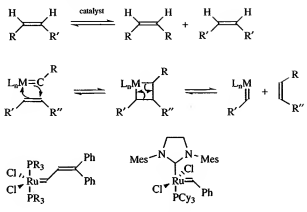


Figure 17. Olefin metathesis reaction and mechanism. (a) and (b) Grubb catalysts.

This is an efficient route to C_{20} polyenes, not easily isolated from natural sources, starting from readily available C_{18} sources.

Metathesis (see Section 7.4) provides a flexible route to longer and shorter chains after reaction at a (usually monoene) double bond.

7.4 Olefin Metathesis

Olefin metathesis is the catalytic exchange of groups attached to a double bond. It presents a number of interesting possibilities for modifying the alkyl chain of fatty acids (Figure 17).

The mechanism involves a [2,2] cycloaddition between a transition metal alkylidene complex and the olefin, resulting in an intermediate metallocyclobutane (103). The metallocycle breaks in the opposite way to give a new alkylidene and a new olefin. Repeated exchange at the metal results in an equilibrium mixture of olefins, usually as an equilibrium mixture of *cis*-and *trans*-isomers. The reaction is used in the petrochemical industry to modify hydrocarbon structure, using catalysts such as $WCl_6/SnMe_4$ or Re_2O_7/Al_2O_3. These catalysts are less active when other functional groups compete for the active site, and the application of metathesis in oleochemistry has paralleled development of novel catalysts, such as Grubb catalysts, containing sterically hindered metal alkylidenes (Figure 17a,b).

Self-metathesis describes the reaction of an unsaturated fatty acid with itself. For example, methyl oleate gives a mixture of starting material (50%), unsaturated hydrocarbon (25%), and long-chain unsaturated diester (25%), all as a mixture of *cis*-and *trans*-isomers. (Figure 18). The diester can be converted to the musk component civetone, but a more efficient route is through self metathesis of the ketone oleon derived from methyl oleate by Claisen condensation (104) (Figure 18).

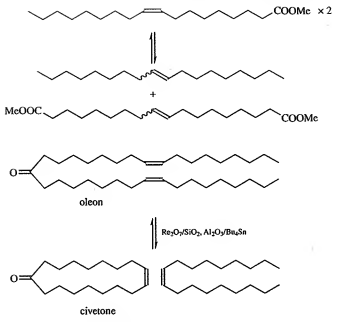


Figure 18. *Self-metathesis reactions.*

Cross-metathesis of an unsaturated fatty ester with a normal alkene is a versatile way of producing chain-shortened or chain-extended homologues leading to oleochemicals with chain lengths outside the C_{16}–C_{22} range of most commodity oils. Methyl oleate reacts with hex-3-ene, in large excess to suppress self-metathesis and push the reaction toward the C_{12} ester and hydrocarbon products. ω-Olefins may be chain extended similarly, the ethene produced being removed to drive the reaction to completion. Cross metathesis provides a route to compounds otherwise difficult to obtain, for example, triacontanol from reduction of the product from methyl erucate and 1-octadecene. Ethenolysis (cross-metathesis with ethene) produces shorter chain ω-olefins with a wide range of applications. A high pressure of ethene is used to force the reaction to the desired products. ω-Olefins produced either by metathesis or from pyrolysis of castor oil can be coupled to give long-chain dibasic acids (105).

Metathesis of intact oils produces polymeric products resulting from intra- and intermolecular bond formation, and they can be used to produce high-viscosity stand oils from drying oils without the loss of double bonds that occurs on thermal polymerization. Vegetable oils can be metathesized efficiently at low temperature and pressure using Grubb's ruthenium catalyst $(Cy_3P)_2Cl_2Ru{=}CHPh$, without the rigorous exclusion of water and oxygen required with $WCl_6/SnMe_4$ (106). Pretreatment of the oil with silica gel may be required.

As a reaction with 100% atom efficiency achieved at moderate temperature (<100°C) using renewable resources, metathesis has potential in a sustainable

chemical industry. A recently developed catalyst (Figure 17b) has an efficiency that justifies industrial application in the production of fine chemicals (106). The hydrocarbon byproducts of metathesis, for example, α-olefins, are also valuable starting materials. Metathesis in oleochemistry, in the context of green chemistry, has recently been reviewed (107).

8. NOVEL CHEMISTRY FOR FUNCTIONALIZING THE ALKYL CHAIN

Oils and fats are renewable resources for the chemical industry. Increasing the range of oleochemicals that can be produced could add value to existing crops and provide a market for new crops, driving research into novel fatty acid derivatives. Most current oleochemical production involves reaction at the carboxyl group, with the chain length and unsaturation of the alkyl chain chosen to give the desired melting behavior or hydrophobicity. Introducing functionality to the alkyl chain through radical, electrophilic, nucleophilic, pericyclic, and transition metal catalyzed addition to carbon–carbon double bonds leads to novel compounds with commercial potential. Only a small selection of recent research is illustrated here, focusing on three promising approaches: neighboring group participation, Friedel Crafts acylation, and free-radical addition reactions.

Functionalizing the alkyl chain places more emphasis on the structure of the fatty acids used as feedstock. Model reactions use single fatty acids, often monoenes with particular double-bond positions. Large-scale use of these reactions needs oils rich in single fatty acids to maintain the purity of the product and minimize wasteful side reactions. Suitable feedstocks may be current crops such as high oleic or high erucic varieties or new crops with unusual fatty acids (Chapter xx). Petroselenic acid (18:1 6c) from umbelliferae oils and 5-eicosenoic acid (20:1 5c) from meadowfoam oil are of particular interest as distinctive products can result from neighboring group participation. Breeding to increase the monoene content of some oils may be desirable. ω-Olefins are useful starting materials; 10-undecenoic acid is available from pyrolysis of castor oil, and others may be produced by metathesis (see Section 7.4). Recent, wide-ranging reviews of this area are available (4, 5, 108)

8.1. Neighboring Group Participation

Neighboring group participation is the involvement of a nearby functional group in the reaction of another functional group. It may influence the regioselectivity of the reaction or lead to specific products, often as a result of cyclization to five-and six-membered rings. Neighboring group participation reactions of fatty acids were reviewed recently (109) and can be used to introduce mid-chain functionality, including heterocyclic groups. Double bonds and the carboxyl group usually react independently of each other, but Δ4 and Δ5 bonds may interact with the carboxyl through neighboring group participation leading to γ- and δ-lactones (five- and

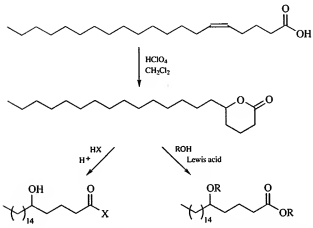


Figure 19. Neighboring group participation leading to lactones and other products from Δ5 acids. X = OH, RO, or RNH.

six-membered rings, respectively). The Δ5 acids from meadowfoam oil readily form lactones when refluxed with perchloric acid. The proportion of δ- and γ-lactones depends on the solvent: 6:1 in hexane and 40:1 in dichloromethane. The δ-lactone is formed faster, but the γ-lactone is the more thermodynamically stable isomer. High dilution and a nonparticipating polar solvent that stabilizes the intermediate cation favor kinetic control of the reaction (110). The lactones can be ring opened by treatment with water, alcohols, and amines in acid, giving 4- and 5-hydroxy acids, esters, and amides (111); alternatively, treatment with an alcohol and a Lewis acid catalyst under more vigorous conditions results in an alkyl group ether linked to the chain (112) (Figure 19).

8.2. Friedel Crafts Acylation

Friedel Crafts acylation with an acyl chloride and Lewis acid catalyst is more often associated with aromatic compounds. Ethylaluminium dichloride ($EtAlCl_2$) is an effective catalyst for the acylation of aliphatic olefins, including fatty acids and alcohols, giving β,γ-unsaturated ketones (113). The reaction occurs with both terminal and internal double bonds, with the acyl group becoming attached to one of the double-bond carbons while the double bond migrates one carbon. Reaction at terminal olefins is regiospecific with addition to the terminal carbon giving a linear product and a predominantly *trans*-double bond. Internal double bonds give an approximately equal mixture of *trans*-regioisomers (Figure 19). α,β-Unsaturated acid chlorides give allyl vinyl ketones that undergo Nazarov cyclization to prostaglandin- and jasmonate-like molecules (Figure 20) (114). Neighboring group participation in petroselenic acid (18:1 6*c*) leads to intramolecular cyclization (115). Friedel Crafts acylation is a flexible route to new and highly functionalized oleochemicals containing reactive allyl keto functions (115).

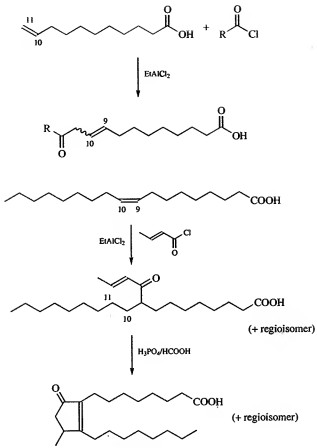


Figure 20. Friedel Crafts acylation reactions.

8.3. Free Radical Addition Reactions

Double bonds participate in free radical addition reactions, and these can be of synthetic use in introducing functional groups (116). A particularly simple reaction is the preparation of γ-lactones by solvent-free addition of 2-halocarboxylates to fatty esters, catalyzed by commercial copper powder at 100–130°C (117). Iodides are most reactive and can be prepared in situ from more readily available bromides and sodium iodide (Figure 21).

Perfluoro alkyl iodides add to both terminal and internal double bonds when the reaction is initiated by electron transfer from metals such as finely divided silver, copper powder, and lead with copper acetate. Using an ω-olefin and a perfluoroalkyl-α,ω-diiodide, a perfluoro group can be inserted into a long-chain compound (118) (Figure 21). Deiodination of the product by catalytic reduction results in highly hydrophobic alkyl chains with interesting surfactant properties.

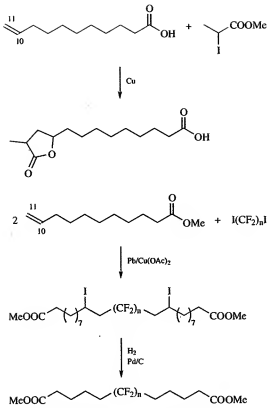


Figure 21. *Radical addition reactions.*

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